Lyme borreliosis

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Abstract

Lyme borreliosis is a tick-transmitted spirochaetal disease caused by *Borrelia burgdorferi sensu lato*. It is acquired in forested and heathland areas of the temperate northern hemisphere. The most common presentation is an erythematous rash spreading slowly from the site of a tick bite. Clinical manifestations of disseminated infection include facial palsy, viral-like meningitis, radiculopathy, meningoencephalitis and arthritis. Lyme borreliosis responds to antibiotic treatment at all stages, with excellent results for patients with early disease. Patients with long-standing infection causing significant tissue damage can have slow or incomplete recovery. A small minority of treated patients can have persistent non-specific symptoms, similar to those seen following some other infections. Controlled trials in patients with post-Lyme symptoms have shown no evidence of persistent infection and no sustained benefit from prolonged antibiotic treatment. Prevention measures focus on tick and disease awareness, avoidance of tick-infested areas where possible, insect repellent use and frequent skin inspections for attached ticks, as early removal minimizes infection risk. No vaccine is currently available.

Keywords acrodermatitis chronica atrophicans; *Borrelia burgdorferi*; erythema migrans; facial palsy; Lyme arthritis; Lyme borreliosis; meningitis; neuroborreliosis; radiculopathy

What's new?

- Recent treatment trials of European patients with early Lyme borreliosis, incorporating non-infected controls, have shown excellent long-term outcomes with no excess of symptoms in cases over controls at 6 months and longer
- Long-term follow-up of patients with neuroborreliosis in a 14-day treatment trial shows oral doxycycline (200 mg daily) to be non-inferior to intravenous ceftriaxone (2 g daily). Poorer outcomes occurred in patients with longstanding pre-existing disease
- Antibody tests with improved specificity are now widely available, but indiscriminate testing of patients with a very low pre-test probability of Lyme borreliosis continues to contribute to false-positive results and misdiagnosis
- Over-diagnosis and mistreatment remain major concerns, driven by misinformation, especially from the Internet

Lyme borreliosis (Lyme disease) is caused by the tick-borne spirochaete *Borrelia burgdorferi*. Erythema migrans (EM), an early skin lesion, is the most common clinical presentation. The organism can spread, causing various manifestations, including facial palsy, viral-like meningitis, radiculitis and arthritis, usually affecting the knee.

Epidemiology and environmental factors

Lyme borreliosis is the most common tick-borne infection in the temperate northern hemisphere.[1]

Over 24,000 confirmed cases were reported in the USA in 2012, mainly from north-east and mid-Atlantic seaboard states, and north-central and Pacific coast states.[2] There may be over 200,000 European cases annually, with high incidences in parts of southern Scandinavia, central and eastern Europe.[1] About 1200 cases are serologically confirmed annually in the UK.[3] Infection can occur at any age in individuals whose residence, occupation or recreational activities place them at risk of bites from *Ixodes* spp. ticks (deer ticks; sheep ticks), the vectors of *B. burgdorferi*.[1] Bites are frequently unrecognized because they do not usually cause significant pain, irritation or itch. Ticks are common in woodland, heath and moorland but can also live in semi-rural areas bordering large population centres. Infections occur mainly in late spring, early summer and autumn, the peak tick feeding periods.[1] The annual incidence varies, depending on climatic and other factors affecting ticks and human activities in tick habitats.[1] Ixodid ticks can also carry other organisms, including ehrlichiae, babesiae and *B. miyamotoi*, a member of the relapsing fever group of borreliae.[1] Tick-borne encephalitis (TBE) virus, for which a vaccine is available, is prevalent in some parts of Europe, and deer tick virus (DTV), another flavivirus, was recently shown to cause encephalitis in the USA.[1,4] Tick-transmitted co-infections can occur and can cause atypical presentations.

Pathogenesis

At least five *B. burgdorferi* genospecies are pathogenic. Borrelial heterogeneity is significant in organotropism and disease presentation and has implications for vaccine development strategies.[5] Only one genospecies (*B. burgdorferi sensu stricto*) causes human infection in North America and can cause neurological and arthritic complications.[1,2] It is found focally in Europe, but two other genospecies are the main causes of European disease: *Borrelia garinii*, which is particularly associated with neuroborreliosis, and *Borrelia afzelii*, associated with skin manifestations and occasionally with neurological complications.[1,6]

Clinical features

Infection can be asymptomatic. Disease has been customarily divided into three stages, but the process is a continuing pathological evolution rather than having distinct phases. Progression to later-stage disease is not inevitable, even in untreated patients, and late manifestations are now uncommon because of greater recognition and treatment of earlier-stage infection.[1]

Localized infection: EM, a localized red or pink rash appearing after 2–30 days (usually 5–15 days) at the site of a bite is the most common manifestation (Figures 1 and 2).[1,2,7] The rash can be faint, with a more pronounced margin that gradually migrates

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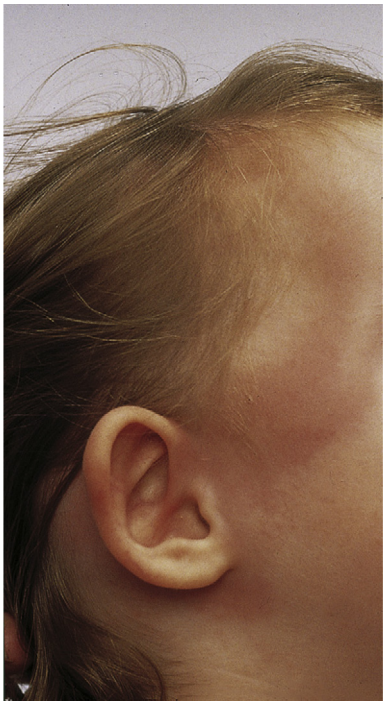

Figure 1 Erythema migrans on the face of a 2-year-old child who had received a tick bite on her scalp 10 days previously.

outwards. A central area of clearing can become evident as previously affected skin returns to normal, but many EM rashes are homogeneous in appearance.[1,7] Local lymphadenopathy can occur. About 80% of patients presenting with later-stage disease recall preceding EM. Borrelial lymphocytoma is a rare localized presentation, usually on the earlobe, nipple or scrotum.[1,7]

Early disseminated infection: the organism can affect many tissues in the following weeks, principally the nervous, musculoskeletal and cardiovascular systems and the skin. Patients can have a flu-like illness with myalgia and arthralgia but without significant respiratory symptoms.[1] Multiple areas of EM can occur but are uncommon in UK-acquired infections. Early neurological presentations include facial palsy, which can be bilateral, other cranial nerve lesions, lymphocytic meningitis and painful radiculoneuritis, which can cause shingles-like pain.[1,7,8]

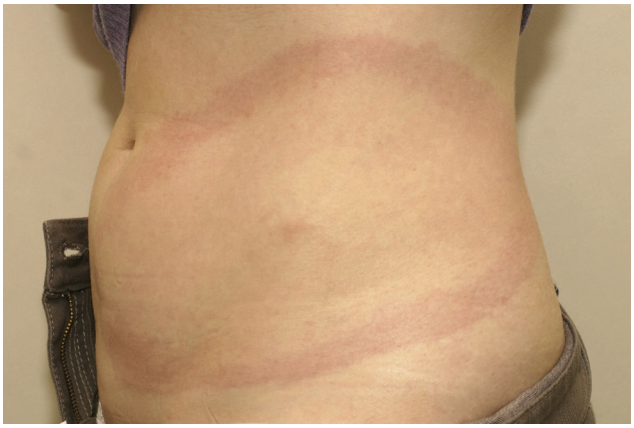

Figure 2 Erythema migrans following a tick bite on the waist several weeks previously (courtesy of Dr B Bovill).

Musculoskeletal complications include persistent arthralgia; recurrent large joint inflammation (usually affecting the knee, and uncommon in UK-acquired infection) can become persistent without antibiotic treatment.[1,7] Cardiac conduction abnormalities are uncommon, usually occurring within a few weeks of infection. Ocular, hepatic and other manifestations have also been reported.[1,7]

Lyme encephalopathy is an uncommon manifestation that can occur with other presentations of disseminated or late infection. Patients complain of poor memory and concentration and have subtle learning difficulties, but do not have clinical, laboratory or imaging evidence of central nervous system infection. The presentation is similar to toxic-metabolic syndromes seen in other systemic inflammatory diseases and gradually resolves following treatment of the infection.[9]

Late encephalomyelitis is rare, estimated to occur in less than one in 1000 previously untreated patients.[9] It is characterized by spastic paraparesis, cognitive impairment, cranial neuropathy, bladder dysfunction and dysarthria.[1,8] There is cerebrospinal fluid (CSF) pleiocytosis and intrathecal antibody production.[8] Appropriate antibiotics will eradicate infection but the degree of recovery depends on the severity of tissue damage prior to treatment.[1,8,10]

Lyme arthritis varies in incidence depending on where the infection has been acquired; it is more common in the USA than in Europe. The degree of joint swelling is usually disproportionate to the pain. In some genetically-predisposed patients, inflammation continues for some time after antibiotic treatment ('antibiotic-refractory' arthritis). A strong antibody response to *B. burgdorferi* is detectable in serum.[1,7]

Acrodermatitis chronica atrophicans is an uncommon late skin manifestation, strongly associated with *B. afzelii*. Lesions usually occur on the limbs and are initially violaceous. If untreated, they last for years, eventually becoming atrophic (Figure 3) and can be accompanied by peripheral neuropathy.[1,7]

Investigations

Diagnosis is primarily clinical, particularly in early disease. Disease awareness can be low in non-endemic areas and the

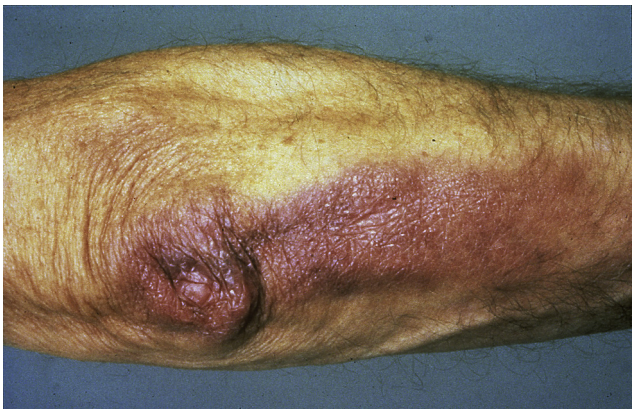

Figure 3 Acrodermatitis chronica atrophicans (courtesy of the late Dr JE White).